UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/581,413 | 06/23/2006 | Kenya Shitara | Q107168 | 1999 |

65565 7590 07/22/2009

SUGHRUE-265550
2100 PENNSYLVANIA AVE. NW
WASHINGTON, DC 20037-3213

| EXAMINER | |
|---|---|
| WEN, SHARON X | |
| ART UNIT | PAPER NUMBER |
| 1644 | |
| MAIL DATE | DELIVERY MODE |
| 07/22/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/581,413 | SHITARA ET AL. | |
| | Examiner | Art Unit | |
| | SHARON WEN | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *04/13/09, 05/11/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *5,6 and 27-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6 and 27-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after Final Rejection. Since this application is eligible for continued Examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/11/2009 has been entered.

2. Applicant's amendment, filed 04/13/2009, has been entered.

Claims 1-4 and 7-26 have been canceled.

Claims 5-6 and 27-46 are pending.

As noted in the previous Office Action, mailed, 12/11/2008, the examination has been extended to **M-CSF**, **IL-2**, **vincristin**, **cyclophosphamide** and **methotrexate** as species of "*agent*", therefore, claims 45 and 46 have been included in the examination. It is noted that the Office Action Summary, mailed 12/11/2008, inadvertently stated that claims 45 and 46 had been withdrawn. Examiner apologizes to the Applicant for any inconvenience on this matter. Furthermore, the examination has been extended to **etoposide** as a species of "*agent*"

Claims 5-6 and 27-46 are currently under examination as they read on a method for treating a CCR4-expressing tumor comprising administering a recombinant antibody that specifically binds chemokine receptor 4 (CCR4).

3. This Action will be in response to Applicant's Arguments/Remarks, filed 04/13/2009.

The rejections of record can be found in the previous Office Actions, mailed 10/17/2007 and 12/11/2008 .

4. The previous rejections under 35 USC 112, first paragraph, have been withdrawn in view of Applicant's amendment, filed 04/13/2009.

Specifically, the deletion of "and/or" in claims 37-38 and 40-41 has obviated the previous enablement rejection for an antibody with fewer than six CDRs. Furthermore, Applicant's Statement of Availability for KM2160 hybridoma, filed 04/13/2009, has obviated the previous rejection on the biological deposit.

5. The previous rejection under 35 USC 102(b) as being anticipated by Shitara et al. (US 2003/0175273 A1) has been withdrawn in view of Applicant's amendment to the claims, filed 04/13/2009.

### *Claim Rejections - 35 USC § 103*

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 5-6 and 27-46 are rejected under 35 U.S.C. 103(a) as being obvious over Shitara et al. (US 2003/0175273 A1, reference of record) in view of Taub (U.S. Patent 6,762,174 B1).

The teaching of Shitara et al. has been discussed in the previous Office Action and is reiterated herein for Applicant's convenience.

Shitara et al. taught a method for treating CCR4-related cancer such as leukemia or lymphoma, which read on hematopoietic organ tumor (given that *hematopoiesis* means the formation of blood cellular components), in which the cancer cells express

CCR4 comprising administering an anti-CCR4 antibody that has antibody-dependent cell-mediated cytotoxicity (ADCC) function (see paragraphs [0019]-[0020], [0030]-[0040], [0070]-[0074], [0230], [0233], [0236] and claims 41-45). The prior art antibody appears to be the same or nearly the same antibody as the instant application with identical CDRs (see paragraphs [0049]-[0050] and SEQ ID NOs: 1-3 and 5-7). In addition, the reference taught the antibody which is a human chimeric antibody or a human CDR-grafted antibody (see abstracted and paragraph [0310]) which read on a recombinant antibody. The prior art also taught that the monoclonal antibody is produced by hybridoma KM2160 (see paragraph [0255]-[0258]). Furthermore, the prior art antibody binds to the same CCR4 epitope as recited in the present claims (see paragraphs [0033]-[0036]. Given the same or nearly the same antibody (i.e., having the same CDRs and produced by the same hybridoma), the prior art antibody would necessarily not have an activity of inhibiting binding of TARC or MDC as a CCR4 ligand to CCR4. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.,* 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

Shitara et al. differs from the present claims in that it did not specifically teach the antibody used in the claimed method which is not conjugated to at least one agent. However, Shitara et al. taught a medicament comprising the antibody as the active ingredient and that the antibody can be administered alone or in a pharmaceutical formulation (see paragraphs [0070]-[0071] and [0238]). Given that the prior art antibody has ADCC activity, one of ordinary skill in the art would have readily recognized that the antibody does not need to be conjugated to an agent to exert its therapeutic effect (i.e., inducing cytotoxic effect on CCR4-expressing cancer cells).

Although it is not necessarily to conjugate the antibody, one of ordinary skill would be reasonably expected to include an unconjugated therapeutic agent in the medicament comprising the anti-CCR4 antibody for treating cancer wherein the therapeutic agent can be any well-known chemotherapeutic agents such as vincristine, cyclophosphamide, etoposide and methotrexate as evidenced by Taub (see entire

document, in particular, see column 6, second paragraph). In particular, Taub taught that combining a Formula I compound and a well-known anti-cancer agent such as vincristine, cyclophosphamide, etoposide or methotrexate would produce synergism in treating cancer (see column 6, lines 9-26). Therefore, one of ordinary skill in the art, upon reading Taub, would have been motivated to include a therapeutic agent such as vincristine, cyclophosphamide, etoposide or methotrexate in the medicament comprising the anti-CCR4 antibody as the active agent for treating cancer for the advantage of synergism (e.g., decreasing dose-limiting side effects).

Given that Shitara et al. taught that the anti-CCR4 antibody has ADCC activity and can be administered alone and the teaching by Taub in that well-known chemotherapeutic agents such as vincristine, cyclophosphamide, etoposide or methotrexate, when combined with an anti-cancer compound, would yield synergism in treating cancer, it would have been obvious to one of ordinary skill in the art to combine the anti-CCR4 antibody with a chemotherapeutic agent such as vincristine, cyclophosphamide, etoposide or methotrexate that is not conjugated to the antibody because the antibody by itself has ADCC activity.

One of ordinary skill in the art would have been equally motivated to include a cytokine, such as G-CSF, M-CSF or IL-2, in the medicament comprising anti-CCR4 antibody for treating CCR4-related cancer because these cytokines are known to activate immune cells (see Shitara et al., paragraph [0163]). Therefore, the ordinary skilled artisan would have been motivated to use these as the additional agent in the medicament to boost the patient's immunity against cancer. It would have been equally obvious to one of ordinary skill in the art not to conjugate the cytokine to the antibody because the antibody has ADCC activity by itself, thus making conjugation unnecessary.

Given the above discussion, the invention, as a whole, was *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made as evidenced by the references, especially in the absence of evidence to the contrary.

***Double Patenting***

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 5-6 and 27-46 are *provisionally* rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 54, 57-70, 74-75 and 81-84 of copending application, USSN 11/969,555 in view of Shitara et al. (US 2003/0175273 A1) and Taub (U.S. Patent 6,762,174 B1). Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of the claims are drawn to the method of treating CRR4-related blood cancer which reads on hematopoietic organ tumor (given that *hematopoiesis* means the formation of blood cellular components) comprising administering the same or nearly the same anti-CCR4 antibody that has ADCC activity. It is noted that anti-CCR4 antibody recited in both sets of the claims have identical CDRs and HV and LV regions (see Table shown below; identical sequences are listed in each row). Furthermore, given that both of the recited antibodies have ADCC activity, it would have been obvious to one of ordinary skill in the art to include a therapeutic agent or a cytokine in the pharmaceutical

composition comprising the antibody but not conjugated to the antibody for the same purpose of treating cancer in view of Shitara et al. and Taub (see above 103 for detailed discussion). In particular, both Shitara and Taub taught well-known chemotherapeutic agents such as vincristine, cyclophosphamide, etoposide and methotrexate to be incorporated in cancer therapy in addition to the active ingredients. Shitara et al. also taught cytokines such as G-CSF, M-CSF and IL-2 have immune cell-activating activity. Therefore, one of ordinary skill in the art would have been motivated to include one of these cytokines or one of these chemotherapeutic agents in the cancer therapy for boosting immune response or achieving synergism in treatment. As such, the two sets of claims render obvious of each other.

| USSN 10/581,413 | USSN 11/094,718 |
|---|---|
| SEQ ID NO: 5 | SEQ ID NO: 14 |
| SEQ ID NO: 6 | SEQ ID NO: 15 |
| SEQ ID NO: 7 | SEQ ID NO: 16 |
| SEQ ID NO: 8 | SEQ ID NO: 17 |
| SEQ ID NO: 9 | SEQ ID NO: 18 |
| SEQ ID NO: 10 | SEQ ID NO: 19 |
| SEQ ID NO: 16 | SEQ ID NO: 27 |
| SEQ ID NO: 17 | SEQ ID NO: 28 |
| SEQ ID NO: 18 | SEQ ID NO: 35 |

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-

3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571)272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/
Examiner, Art Unit 1644
July 15, 2009